OVARIAN COMPENSATORY HYPERTROPHY FOLLOWING UNILATERAL OVARIECTOMY IN THE SUCKLED SOW


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ABSTRACT

The effects of unilateral ovariectomy on ovarian compensatory hypertrophy (OCH), endocrine profiles and the pituitary response to gonadotropin releasing hormone (GnRH) were studied in 46 multiparous suckled sows. On d 20 of lactation (d 0 of experiment), sows were subjected to sham ovariectomy (Sham; n = 23) or unilateral ovariectomy (ULO; n = 23). On d 1 (n = 16), 2 (n = 15) or 8 (n = 15) following initial surgery the remaining ovaries in both Sham and ULO sows were removed. Immediately following removal of the remaining ovaries, GnRH (10 μg) was administered to each sow. Peripheral blood samples were taken every 10 min for 80 min beginning 20 min prior to GnRH administration. No difference in ovarian weight was observed between ULO and Sham sows until d 8, when ovarian weight was greater (P<.05) for the remaining ovary from ULO sows (3.96 ± .21 vs 5.91 ± .39 g). Ovarian follicular fluid weights from ULO sows were greater (P<.05) than Sham sows on both d 2 and 8. On d 1, plasma concentrations of follicle stimulating hormone (FSH) were greater (P<.05) in ULO sows than in Sham sows (2.9 ± .2 vs 2.1 ± .1 ng/ml). Plasma FSH concentrations, however, did not differ between Sham and ULO sows on either d 2 or 8. Ovarian venous concentrations of estradiol-17β were also greater (P<.05) in ULO sows compared with Sham sows on d 2 but not d 8. Treatment mean differences for both plasma concentrations of luteinizing hormone (LH) and the pituitary LH response to GnRH were not significant. No difference in pituitary FSH response to GnRH was observed between ULO and Sham sows on either d 1 or 2 following initial surgery. However, Sham sows released more (P<.05) FSH than ULO sows on d 8. These results indicate that OCH was evident in the suckled sow by 2 d after ULO. Furthermore, OCH was characterized by an acute, but short-lived, increase in plasma concentrations of FSH and ovarian venous concentrations of estradiol-17β.

(Key Words: Pigs, Reproduction, Lactation, Follicles.)

Introduction

It has been shown in the gilt that ovarian compensatory hypertrophy (OCH) occurs following unilateral ovariectomy (ULO) before puberty (Dailey et al., 1970; Redmer et al., 1984), during the estrous cycle (Wiginton et al., 1979) and during pregnancy (Rexroad and Casida, 1976). In the cyclic and pregnant gilt, OCH has been characterized by an increase in follicular fluid volume (Rexroad and Casida, 1976) or increased ovulation rate in the remaining ovary (Wiginton et al., 1979). In the prepuberal gilt ULO is followed by elevations in peripheral and ovarian venous concentrations of follicle stimulating hormone (FSH) and estradiol-17β, respectively (Redmer et al., 1984). Recent evidence suggests that OCH may be due either to an acute increase in plasma FSH concentration or a decline in circulating inhibin concentration immediately following ULO (rat: Butcher, 1977; Welschen et al., 1978; DePaolo et al., 1981; pig: Redmer et al., 1984).

In the suckled female the effects of ULO have not been well established. Suckling in the ULO rat appears to inhibit OCH (Mena et al., 1974), while in the ULO cow suckling apparently has little effect on OCH (England et al., 1973). The present study was undertaken to determine whether the suckled sow is capable of exhibiting OCH following ULO and to characterize the effect of ULO on peripheral plasma FSH and luteinizing hormone (LH) concentrations, ovarian venous concentrations of estradiol-17β and the pituitary response to gonadotropin releasing hormone (GnRH).

Materials and Methods

Sows utilized in this experiment were multiparous and represented four-way crosses of
Yorkshire-Landrace × Chester White-Large White breeds. All sows were housed in individual lactation stalls and maintained on a corn-soybean-based lactation diet. Forty-six sows were assigned to one of two groups on d 20 of lactation (d 0): sham ovariectomy (Sham) or ULO. Sows were anesthetized with sodium thiopental (1 g) and anesthesia was maintained with a closed circuit system of halothane and oxygen. The surgical procedure utilized on d 0 in sows comprising the ULO group consisted of removal of one ovary through an upper lumbar incision. Sham sows were subjected to a similar procedure without ovariectomy.

Following recovery on d 0, sows were returned to their respective lactation stalls to continue nursing litters. Litters were adjusted so that each sow nursed between six and ten piglets. Both groups were then subdivided and sows were subjected to a second laparotomy on d 1, 2 or 8 after the initial surgery. The remaining ovary from ULO sows and both ovaries from Sham sows were removed.

Immediately following ovariectomy, all ovaries were weighed to determine total ovarian weight, then pressed to remove follicular fluid and reweighed. The difference between the total and pressed ovarian weights was defined as the follicular fluid weight. Pressed ovaries were then dried in a convection oven at 45 °C for 24 h to determine dry weight.

At second laparotomy a cannula was inserted into the jugular vein by procedures described by Ford and Maurer (1978). Blood samples (10 ml) were collected at −20 min, −10 min and immediately before ULO (0 min) on d 1, 2 or 8. Immediately following total ovariectomy, 10 μg GnRH was infused via the indwelling jugular cannula. The cannula was then flushed with 10 ml of physiological saline. Blood samples were collected in heparinized tubes at 10, 20, 30, 40, 50 and 60 min following GnRH administration. All blood samples were centrifuged at 1,200 × g for 10 min and the plasma frozen at −20 °C.

Hormone Analyses. Plasma LH concentrations were determined by a double antibody radioimmunoassay described by Niswender et al. (1969) using rabbit anti-porcine LH (#566) as first antibody, sheep anti-rabbit gamma globulin as second antibody and purified porcine LH (LER-786-3) as labeled tracer and standard. Intra- and inter-assay coefficients of variation of LH assays were 11.2 and 21%, respectively.

Plasma concentrations of FSH were also determined by a double antibody radioimmunoassay previously described by Niswender et al. (1969) for LH. Anti-porcine FSH antibody (1533) prepared in rabbits and specific against the porcine FSH beta subunit was used at an initial dilution of 1:8,300 (Redmer et al., 1984). Sheep anti-rabbit gamma globulin served as the second antibody and purified pFSH (IIA3-c2) was used as the labeled tracer and standard. The FSH mean concentration (± SE) was 5.4 ± 0.13 ng/ml (coefficient of variation = 7.8%). Between-assay variation was 8.4%.

The estradiol-17β (E2) radioimmunoassay used was previously described by Kesler et al. (1977) and validated for swine by Redmer and Day (1981). The intra-assay coefficient of variation was 5.4%.

Statistical Analyses. Data for ovarian and hormonal variables were analyzed by least-squares analysis of variance with treatment mean comparisons among days evaluated by the protected least significant difference (LSD) test (Snedecor and Cochran, 1980).

The magnitude of FSH and LH responses to GnRH treatment was estimated by measuring the cumulative increase in plasma content of hormone after GnRH treatment. The accumulated area established by the six plasma values obtained following GnRH administration was defined as total area. Subtraction of baseline area (three pre-treatment samples) from total area yielded the cumulative increase (ng/ml). Response differences were analyzed by least-squares analysis of variance.

Results

Treatment × day interaction in total ovarian and follicular fluid weight was significant. A linear increase in total ovarian weight and follicular fluid weight occurred over time in ULO sows, while no increase was evident in Sham sows (table 1). Total ovarian weight did not differ (P > .05) between Sham and ULO sows until d 8. Follicular fluid weight, however, was

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TABLE 1. TOTAL OVARIAN AND FOLLICULAR FLUID WEIGHT IN SHAM AND UNILATERALLY OVARIECTOMIZED (ULO) SUCKLED SOWS

<table>
<thead>
<tr>
<th>Item</th>
<th>Ovarian wt</th>
<th>Follicular fluid wt</th>
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<tr>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>g</td>
<td>g</td>
</tr>
<tr>
<td>Ovarian wt</td>
<td>ULO$^b$</td>
<td>Sham$^c$</td>
</tr>
<tr>
<td></td>
<td>3.80 ± .53$^{e}$ (8)$^d$</td>
<td>4.37 ± .60$^{e}$ (8)</td>
</tr>
<tr>
<td></td>
<td>4.32 ± .34$^{e}$ (8)</td>
<td>3.91 ± .29$^{e}$ (7)</td>
</tr>
<tr>
<td>Follicular fluid wt</td>
<td>ULO$^b$</td>
<td>Sham$^c$</td>
</tr>
<tr>
<td></td>
<td>1.56 ± .32$^{g}$ (8)</td>
<td>2.22 ± .32$^{g}$ (8)</td>
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<td></td>
<td>1.81 ± .14$^{g}$ (8)</td>
<td>1.41 ± .11$^{g}$ (7)</td>
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</tbody>
</table>

$^a$Number of days following Sham or ULO performed on d 20 of lactation.
$^b$Mean of remaining ovaries.
$^c$Mean of both ovaries.
$^d$Values in parentheses are number of observations.
$^{e,f,g,h}$Means (± SE) within the same column or row that do not have a common superscript differ (P<.05).

greater (P<.05) in ULO sows on both d 2 and 8, with the largest difference observed on d 8. Treatment means in ovarian dry weight were not different between Sham and ULO sows (.52 ± .03 vs .55 ± .03, respectively; mean = .54 ± .04 g).

Ovarian venous estradiol (E$_2$) concentrations were greater (P<.05) in ULO than Sham sows on d 2 (table 2). Ovarian venous E$_2$ decreased by d 8 in ULO sows to values similar (P>.05) to those of Sham sows.

Peripheral plasma concentrations of FSH on d 1 were greater (P<.05) in ULO than Sham sows (figure 1). FSH concentrations did not differ between ULO and Sham sows on either d 2 or 8. Changes in peripheral plasma concentrations of LH were similar (P>.10) in Sham and ULO sows (table 3).

A significant treatment × day interaction revealed a tendency for the FSH response to GnRH treatment in ULO sows to decrease over time, while in Sham sows the FSH response tended to increase over time (table 4). The FSH response was not different between ULO and Sham sows on either d 1 or 2. On d 8, however, Sham sows released more (P<.05) FSH than controls in response to GnRH treatment. There were no significant differences between ULO and Sham sows in the mean LH response to GnRH on d 1, 2 or 8.

Discussion
The present study demonstrates that the remaining ovary of the suckled sow undergoes compensatory hypertrophy in response to the

TABLE 2. OVARIAN VENOUS PLASMA ESTRADIOL CONCENTRATION (PG·ML$^{-1}$·OVARY$^{-1}$) IN SHAM AND UNILATERALLY OVARIECTOMIZED (ULO) SUCKLED SOWS

<table>
<thead>
<tr>
<th>Treatment</th>
<th>1</th>
<th>2</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>ULO</td>
<td>ID$^b$</td>
<td>105 ± 20$^d$ (7)$^e$</td>
<td>45 ± 13$^e$ (6)</td>
</tr>
<tr>
<td>Sham</td>
<td>87 ± 19$^{de}$ (7)</td>
<td>45 ± 21$^e$ (6)</td>
<td>54 ± 18$^{de}$ (7)</td>
</tr>
</tbody>
</table>

$^a$Number of days following ULO performed on d 20 of lactation.
$^b$Insufficient data collected.
$^c$Values in parentheses are number of observations.
$^{d,e}$Means (± SE) within the same column or row that do not have a common superscript differ (P<.05).
removal of the contralateral ovary. These results are comparable to those obtained by Redmer et al. (1984) and Wiginton et al. (1979) in the prepuberal and cyclic gilt, respectively.

Concomitant increases in follicular fluid weight and E2 output of the remaining ovary were evident by d 2 following ULO. These results are in close agreement with those of Redmer et al. (1984), who reported commensurate increases in the same traits following ULO in the prepuberal gilt.

A significant increase in follicular fluid weight of the remaining ovary reflects increased follicular development by that ovary. Whether this increase was due to a change in follicle numbers, follicle size, the rate of atresia or a combination of all three, was not determined. However, the following observations suggest that decreased follicular atresia following ULO should be considered as a probable cause of OCH in the suckled sow.

First, the ovaries of the suckled sow differ from those of the cyclic gilt with regard to large follicles (>5 mm diameter). Although follicle numbers and size were not recorded, it was observed that large follicles were absent from most ovaries removed from suckled sows on d 0 (d 20 of lactation). Thus, OCH can not be attributed only to an increase in the growth rate of large follicles on the remaining ovary in the lactating sow. Second, a comparison of normal and atretic follicles during late lactation in intact sows revealed that the rate of atresia gradually decreases in sows as lactation progresses (Kunavongkrit et al., 1982). Because a decrease in the rate of atresia appears to be an intrinsic phenomenon characteristic of the lactating sow, it may be that ULO initiates OCH by decreasing follicular atresia in the remaining ovary even to a greater extent.

The present study shows a significant increase in follicular fluid weight 2 d after ovariectomy accompanied by an increase in ovarian venous concentration of E2. Redmer et al. (1984) also recorded concomitant increases in ovarian venous E2 and follicular fluid weight of the remaining ovary 2 d after ULO in the prepuberal gilt. The elevation in E2 output by the remaining ovary may have resulted from increased FSH secretion which occurred by d 1 following ULO. A post-ULO rise in FSH has been documented in the rat (Benson et al., 1969; Butcher, 1977) and hamster (Bast and Greenwald, 1977). In the prepuberal gilt, Redmer (1983) reported elevated ovarian venous concentrations of E2 by d 2 after ULO, but no

Table 3. Peripheral Plasm LH Concentrations (ng/ml) in Sham and Unilaterally Ovariectomized (ULO) Suckled Sows (± SE)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>ULO</td>
<td>.9 ± .2 (8)</td>
<td>1.0 ± .3 (8)</td>
<td>.8 ± .2 (7)</td>
</tr>
<tr>
<td>Sham</td>
<td>1.2 ± .4 (8)</td>
<td>1.2 ± .2 (7)</td>
<td>1.2 ± .3 (8)</td>
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</table>

*Number of days following sham or ULO performed on d 20 of lactation.

*Values in parentheses are number of observations.
TABLE 4. CUMULATIVE INCREASE (NG/H) IN PLASMA CONTENT OF LH AND FSH OVER BASE LEVEL FOLLOWING GnRH ADMINISTRATION IN SHAM AND UNILATERALLY OVARIECTOMIZED (ULO) SUCKLED SOWS

<table>
<thead>
<tr>
<th>Item</th>
<th>1</th>
<th>2</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>LH response</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ULO</td>
<td>56 ± 12&lt;sup&gt;cd&lt;/sup&gt; (8)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>47 ± 14&lt;sup&gt;de&lt;/sup&gt; (8)</td>
<td>81 ± 10&lt;sup&gt;e&lt;/sup&gt; (7)</td>
</tr>
<tr>
<td>Sham</td>
<td>41 ± 12&lt;sup&gt;d&lt;/sup&gt; (8)</td>
<td>46 ± 6&lt;sup&gt;de&lt;/sup&gt; (7)</td>
<td>75 ± 10&lt;sup&gt;e&lt;/sup&gt; (8)</td>
</tr>
<tr>
<td>FSH response</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>ULO</td>
<td>47 ± 6&lt;sup&gt;d&lt;/sup&gt; (8)</td>
<td>42 ± 12&lt;sup&gt;de&lt;/sup&gt; (8)</td>
<td>21 ± 9&lt;sup&gt;d&lt;/sup&gt; (7)</td>
</tr>
<tr>
<td>Sham</td>
<td>28 ± 8&lt;sup&gt;d&lt;/sup&gt; (8)</td>
<td>36 ± 9&lt;sup&gt;d&lt;/sup&gt; (7)</td>
<td>49 ± 8&lt;sup&gt;g&lt;/sup&gt; (8)</td>
</tr>
</tbody>
</table>

<sup>a</sup>Number of days following Sham or ULO.
<sup>b</sup>Values in parentheses are number of observations.
<sup>c,d,e</sup>Means (± SE) within the same column or row that do not have a common superscript differ (P<.05).

Concomitant increase in plasma FSH concentrations on d 2. In a later study, however, more frequent blood sampling revealed that plasma FSH concentrations were significantly elevated by 24 h after ULO (Redmer et al., 1984). Thus, an FSH-Eprogesterone cause and effect relationship following ULO may exist in both the repuberal gilt and the suckled sow.

In the present study, elevated ovarian venous E<sub>2</sub> concentrations in ULO sows on d 2 appear to be the result of a post-ULO rise in FSH. Studies have shown that FSH binds almost exclusively to granulosa cells (Midgley, 1973), granulosa cells are a primary source of E<sub>2</sub> (Dorrington et al., 1975; Moon et al., 1978) and FSH administration to cultured granulosa cells increases their production of E<sub>2</sub> (Dorrington et al., 1975; Funkenstein et al., 1980; Evans et al., 1981). The decline in ovarian venous E<sub>2</sub> concentrations by the remaining ovary on d 8 may be due either to decreased plasma concentrations of FSH or a decrease in the ability of FSH to bind to granulosa cells. In this study, no significant decrease in FSH concentration was observed following ULO. Therefore, decreased ovarian venous concentrations of E<sub>2</sub> by d 8 appear to result from suppressed FSH binding to granulosa cells.

The factor responsible for suppression of FSH binding to granulosa cells may be FSH binding inhibitor. While inhibition of FSH secretion and(or) release from the pituitary has been attributed to inhibin (DePaolo et al., 1979; Sato et al., 1980), it seems that FSH binding inhibitor acts at the ovary, specifically the granulosa cells (Sato et al., 1980, 1982). Darga and Reichert (1978) have shown that FSH binding inhibitor is capable of suppressing FSH binding to porcine granulosa cells in vitro. Furthermore, it is known that FSH inhibitor(s) is a product of follicular origin, produced specifically by the granulosa cells (Sato and Ishibashi, 1982). Therefore, ULO may have temporarily decreased circulating concentrations of FSH inhibitors, resulting in an increase in plasma concentration and(or) binding of FSH and ovarian follicular growth. However, by d 8 following ULO it is likely that increases in follicular growth exhibited by the remaining ovary also resulted in an increase, or compensation, in that ovary’s production of FSH inhibitor(s). This, in turn, re-established suppression of FSH stimulation at the ovary, which was reflected in decreased ovarian venous E<sub>2</sub> concentrations.

Data from the present study indicate that an acute increase in FSH that is not accompanied by a concurrent rise in LH occurs following ULO in the suckled sow. These results agree with those of Redmer et al. (1984) for the prepuberal pig and Welschen et al. (1978) and Butcher (1977) for the cyclic rat. In addition, it was also apparent that ULO in the suckled sow had no effect on the pituitary LH response to GnRH treatment.

Results from the present study also show that the FSH response to GnRH treatment was not different between ULO and Sham sows 1 d after ULO. If FSH inhibitor (inhibin) does act at the pituitary to suppress FSH release, one would expect a decrease in this inhibition immediately following ULO to result in a significant increase in the amount of FSH released following GnRH.
on either d 1 or 2 following ULO. According to Redmer (1983), charcoal-treated porcine follicular fluid is capable of suppressing the FSH response to GnRH treatment in a dose-dependent manner. More importantly, Redmer (1983) further demonstrated that the suppressive effect of porcine follicular fluid could be overcome by increasing the dose of GnRH. Hence, it is also possible that 10 µg of GnRH administered to suckled sows in the present study may have been excessive and sufficient to conceal changes in the pituitary FSH response on day 1, 2 and 8 following ULO.

The decreased FSH response to GnRH exhibited by ULO sows on d 8 may be due to depleted pituitary stores of FSH. In the present study, plasma concentrations of FSH were significantly higher on d 1 following ULO and did not change throughout the duration of the study. The elevated plasma FSH concentrations in ULO sows may have resulted from the release of additional pituitary stores of FSH that were not subsequently replaced. Crighton and Lamming (1969) have demonstrated that the pituitary gland of the suckled sow is incapable of increased LH synthesis under circumstances when the pituitary of the cyclic sow is capable of doing so. It is possible that the inability of the sow to increase pituitary LH synthesis during lactation may extend to FSH synthesis as well.

In summary, these data demonstrate that the remaining ovary of the suckled sow will compensate after ULO. Initial changes following ULO include increased follicular fluid weight of the remaining ovary, along with concomitant increases in concentrations of ovarian venous E2 and plasma FSH. As growth of the hypertrophic ovary progresses, changes in ovarian venous E2, FSH and, perhaps, the FSH response to GnRH may be attributed to changes in the production of a non-steroidal factor of follicular origin. Finally, these results suggest that the response to ULO in the suckled sow is similar to that previously described for the prepuberal gilt.

**Literature Cited**


